

simulation and experimental results are shown for 1–4 injection points for antisolvent. As can be seen, a good agreement is found between the simulation and experimental data. In particular, the location of the peak and width of the final CSD is captured reasonably well. The mean crystal size is found to be 67, 80, 94 and 106 μm for 1, 2, 3 and 4 points of antisolvent addition, respectively. For one injection point where all the antisolvent is added at the inlet, a large number of small crystals is created due to nucleation leading to smaller mean size of the product crystals. For two injection points, 50% of the antisolvent is added in the inlet. This results in lower supersaturation compared to the one injection point and therefore fewer number of small crystals were generated due to nucleation. The remaining 50% antisolvent is added to the next addition point. This addition generates supersaturation which is mostly consumed by growth of the smaller crystals resulting in larger crystals compared to the previous case. For three and four injection points, similar mechanisms are observed by Alvarez and Myerson.²² Ridder *et al.*²⁴ carried out optimization studies for antisolvent crystallization of flufenamic acid using the same kinetic parameters but without considering GRD. They found that equal distribution of the antisolvent among the addition points does not necessarily provide the optimal supersaturation profile along the PFC. In order to maximize the average crystal size and minimize the coefficient of variation (a measure of the variability of crystal size), the optimum antisolvent profile is found to be such that, at the first segment, about 30% of the total antisolvent is added, which generates enough supersaturation so that nucleation occurs. At the second segment almost no antisolvent is added so that the crystals from the first segment can grow in moderate supersaturation without further nucleation. In the subsequent two segments, the remaining 30% and 40% of the total antisolvent is added to facilitate the further growth of the crystals. Su *et al.*²⁵ investigated the design and optimization of the antisolvent crystallization of paracetamol in acetone with water as antisolvent in a PFC. They arrived at the similar conclusion that there are optimum locations and amount of antisolvent additions that avoid excessive nucleation and promote crystal growth resulting in large average crystal size with less variability.

2.5 Numerical Solution Methods for the Population Balance Equations

Various numerical methods were developed and/or applied to solve the PBE. This subsection aims to give a brief overview of the most popular solution techniques, focusing, but not limiting to the one dimensional PBE eqn (2.31).

2.5.1 Moment Based Methods

The standard method of moments (SMOM) is the most widely used solution technique of the PBEs,²⁶ which relies on the moment transformation: